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Dike, Bronstein, Roberts & Cushman  
EDWARDS & ANGELL  
P.O. Box 9169  
Boston, MA 02209

[REDACTED] EXAMINER

WOITACH, JOSEPH T

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. <b>09/091,608</b>	Applicant(s) <b>Bebbington et al.</b>
	Examiner <b>Joseph Woitach</b>	Art Unit <b>1632</b>
<b>-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --</b>		
<b>Period for Reply</b> A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.		
- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).		
<b>Status</b>		
1) <input checked="" type="checkbox"/> Responsive to communication(s) filed on <u>Dec 9, 2002</u>		
2a) <input checked="" type="checkbox"/> This action is FINAL.      2b) <input type="checkbox"/> This action is non-final.		
3) <input type="checkbox"/> Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11; 453 O.G. 213.		
<b>Disposition of Claims</b>		
4) <input checked="" type="checkbox"/> Claim(s) <u>11, 21-24, 28-31, 33-42, 46, 47, and 53</u> is/are pending in the application.		
4a) Of the above, claim(s) _____ is/are withdrawn from consideration.		
5) <input type="checkbox"/> Claim(s) _____ is/are allowed.		
6) <input checked="" type="checkbox"/> Claim(s) <u>11, 21-24, 28-31, 33-42, 46, 47, and 53</u> is/are rejected.		
7) <input type="checkbox"/> Claim(s) _____ is/are objected to.		
8) <input type="checkbox"/> Claims _____ are subject to restriction and/or election requirement.		
<b>Application Papers</b>		
9) <input type="checkbox"/> The specification is objected to by the Examiner.		
10) <input type="checkbox"/> The drawing(s) filed on _____ is/are a) <input type="checkbox"/> accepted or b) <input type="checkbox"/> objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).		
11) <input type="checkbox"/> The proposed drawing correction filed on _____ is: a) <input type="checkbox"/> approved b) <input type="checkbox"/> disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action.		
12) <input type="checkbox"/> The oath or declaration is objected to by the Examiner.		
<b>Priority under 35 U.S.C. §§ 119 and 120</b>		
13) <input type="checkbox"/> Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) <input type="checkbox"/> All b) <input type="checkbox"/> Some* c) <input type="checkbox"/> None of: 1. <input type="checkbox"/> Certified copies of the priority documents have been received. 2. <input type="checkbox"/> Certified copies of the priority documents have been received in Application No. _____. 3. <input type="checkbox"/> Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). *See the attached detailed Office action for a list of the certified copies not received.		
14) <input type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e). a) <input type="checkbox"/> The translation of the foreign language provisional application has been received.		
15) <input type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.		
<b>Attachment(s)</b>		
1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)		
2) <input type="checkbox"/> Notice of Dreftsperson's Patent Drawing Review (PTO-948)		
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Peper No(s). _____		
4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____		
5) <input type="checkbox"/> Notice of Informel Patent Application (PTO-152)		
6) <input type="checkbox"/> Other: _____		

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## **DETAILED ACTION**

This application is a 371 National stage filing of PCT/GB69/03209, filed December 23, 1996.

Applicants amendment filed December 9, 2002, paper number 19, has been received and entered. Claims 11, 21-24, 28, 31, 33, 35 and 53 have been amended. Claims 11, 21-24, 28-31, 33-42, 46, 47 and 53 are pending and currently under examination.

### ***Claim Objections***

Claim 1 and 31 objected to because of minor informalities is withdrawn. Amendments to the claims has obviated the basis of the specific objections.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereto by the applicant for patent.

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Claims 11, 21-24, 28-31, 33-42, 46, 47 and 53 rejected under 35 U.S.C. 102(e) for being anticipated by Roberts (US 5,712,149) is withdrawn.

Claims 11, 21-24, 28-31, 33-42, 46, 47 and 53 rejected under 35 U.S.C. 102(e) for being anticipated by Seed *et al.* (US 5,912,170) is withdrawn.

Claims 11, 21-24, 28-31, 33-42, 46, 47 and 53 rejected under 35 U.S.C. 102(a) as being anticipated or clearly anticipated by Capon *et al.* (WO 96/24671) is withdrawn.

Amendments to the claims to encompass the use of only CDR-grafted antibodies has differentiated the instant claims from that disclosed in each of Roberts, Seed *et al.* and Capon *et al.* Though each of the references teach the use of chimeric antibodies, none of the references specifically teach CDR-grafted antibodies.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

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the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11, 21-24, 28-31, 33-42, 46, 47 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts, Seed *et al.* and Capon *et al.* in view of Adair *et al.* (WO/91/09967).

Roberts discloses a DNA delivery system and effector cells comprising such comprising chimeric receptors and/or cells comprising in reading frame a signal peptide component; an antibody or antigen binding fragment thereof, including spacer regions thereof comprising antibody constant- and/or hinge regions (e.g. col. 6, lines 63-64; col. 8, line 38 through col. 9, line 51; col. 31, cl. 5-6); a transmembrane component, including one from CD28 (e.g. col. 8, lines 22-29) a non-naturally linked cytoplasmic signaling component of CD2 or CD28 (see col. 31, cl. 1) and/or an additional non-naturally linked cytoplasmic signalling component capable of acting cooperatively wherein the cytoplasmic signalling components from CD2 and CD28 and/or others are derived from membrane spanning polypeptides or inherently comprising immunoreceptor tyrosine kinase based activation motifs (e.g Fig. 1D; col. 5, lines 36-41; col. 7, line 46 through col. 8, lines 14; col. 32, cl. 12). Roberts further discloses carriers for delivering the recombinant DNAs comprising viral and non-viral vectors, liposomal vectors (e.g. col. 12, lines 43-54) and effector cells comprising one or more of the above DNAs (see e.g. col. 15, lines 33-56; col. 32, cl. 10; col. 33, cl. 15 and cl. 20).

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Seed discloses a DNA delivery system and effector cells comprising such comprising chimeric receptors and/or cells comprising in reading frame a signal peptide component; an antibody or antigen binding fragment thereof, including spacer regions thereof comprising antibody constant- and/or hinge regions (e.g. col. 28, lines 56 through col. 29, line 62; col. 41, cl. 1); a transmembrane component, including one from CD28 and CD4 (e.g. col. 29, line 63 through col. 30, line 20; col. 31, line 23 through col. 32, line 18 ) a non-naturally linked cytoplasmic signalling component of CD2 or CD28 (see col. 31, cl. 1) and/or an additional non-naturally linked cytoplasmic signalling components capable of acting cooperatively wherein the cytoplasmic signalling components from CD28 or those inherently comprising non-naturally linked immunoreceptor tyrosine kinase based activation motifs (e.g. Fig. 1A; col. 6, line 59 through col. 7, line 26; col. 7, line 60 through col. 8, line 4; 8, lines 29-33; col. 31, lines 54-65; col. 31, line 66 through col. 32, line 7). Seed further discloses the construction of use of vaccinia virus recombinants as carriers to deliver into effector cells (e.g. col. 26, line 23 through col. 27, line 51).

Capon discloses a DNA delivery system and effector cells comprising such comprising chimeric receptors and/or cells comprising in reading frame a signal peptide component; multiple antibody or antigen binding fragments, including spacer regions thereof comprising antibody constant- and/or hinge regions (e.g. p. 11, line 6 through p. 19, line 24; p. 36-43); transmembrane components, including ones derived from the parts of the alpha, beta or zeta chains of the T cell receptor (e.g. p. 24, lines 14-17); non-naturally linked cytoplasmic signalling

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components of CD2 or CD28 and/or an additional non-naturally linked cytoplasmic signalling component capable of acting cooperatively wherein the cytoplasmic signalling components from CD2 and CD28 and/or others are derived from membrane spanning polypeptides or inherently comprising immunoreceptor tyrosine kinase based activation motifs (e.g. p. 21-22). Capon further discloses carriers for delivering the recombinant DNAs comprising viral and non-viral vectors, liposomal vectors (e.g. p. 28, lines 11-21) and effector cells comprising one or more of the above DNAs (e.g. p. 29, lines 5-19).

In summary, each Roberts, Seed *et al.* and Capon *et al.* provide the guidance for a DNA delivery system comprising a DNA construct encoding: (a) a signal peptide; (b) a binding component comprising an recombinant antibody; (c) a transmembrane component; (d) two or more cytoplasmic signalling domains; and (e) one or more spacer regions. However, none of the references specifically teach to use a recombinant antibody which is CDR-grafted antibody as component (b). At the time of filing Adair *et al.* teach CDR-grafted antibodies were known and used to generate humanized antibodies. Adair *et al.* teach that the use of CDR-grafted humanized antibodies allows for the use of the recombinant antibody *in vivo* in a human patient because it avoids the undesirable immune response of an antibody derived uniquely from a different species (page 2, second and third paragraphs). Further, the use of CDR grafting allows for the use of an already identified and useful antibody. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the CDR-grafted antibodies taught by Adair *et al.* as one of the forms of recombinant

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antibodies as the binding component of the DNA delivery system taught by Roberts, Seed *et al.* and Capon *et al.* One having ordinary skill in the art would have been motivated to substitute a CDR-grafted antibody because as Adair et al. teach it avoids undesirable immune responses in the recipient to which it is administered (page 2, third paragraph). Further, the use of the CDR of an antibody allows for the generation of a recombinant humanized antibody from already existing antibodies generated in other species (page 2, fourth paragraph). There would have been a reasonable expectation of success to substitute the recombinant CDR-grafted antibody taught by Adair *et al.* into the system of Roberts, Seed *et al.* and Capon *et al.* given the successful results of Roberts, Seed *et al.* and Capon *et al.* for using other forms of recombinant antibodies.

To the extent Applicants arguments apply to the instant claims, Examiner notes the amendments to the claims to specifically use CDR-grafted antibodies and that Roberts, Seed *et al.* and Capon *et al.* do not specifically teach to use a CDR-grafted antibody (see Applicants amendment, pages 5-6). However, Roberts, Seed *et al.* and Capon *et al.* clearly teach the use recombinant antibodies. As noted by the specification CDR-grafted antibodies were well known form of recombinant antibody at the time of filing (page 6). The use of CDR-grafted antibodies would have been an obvious variation of recombinant antibody for the use in the systems taught by Roberts, Seed *et al.* and Capon *et al.* A review of the present specification does not provide any working examples or indication that the use of CDR-grafted antibodies provides any unexpected property over the use of any other recombinant antibody, therefore a recombinant

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CDR-grafted antibody would be an obvious substitution for the recombinant chimeric antibodies taught by Roberts, Seed *et al.* and Capon *et al.*

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

*Deborah Crouch*  
DEBORAH CROUCH  
PRIMARY EXAMINER  
GROUP 1800 (63)